REMARKS

Claims 1-2, and 4-28 are pending in the application. Claims 11-25 are withdrawn from consideration as being drawn to a non-elected invention. Claim 3 has been canceled without prejudice or disclaimer. Claims 1, 2 and 26 have been amended to better clarify what Applicants believe to be the invention. No new matter has been entered by way of this amendment. Accordingly, claims 1-2, 4-10 and 26 through 28 are currently under consideration. Reconsideration of this application is respectfully requested.

Applicants' representatives would like to express their sincere appreciation for the courteous and constructive telephonic interview held with Examiners Susan Beth McCormick-Ewoldt and Patricia Leith on March 23, 2006, as related to the claims under consideration. As noted in that telephone conversation, the Examiners kindly reviewed the amended claims and suggested canceling the composition claims and filing method claims. Applicants' representative noted that she would discuss this with the inventors.

Rejection under 35 U.S.C. §102

The Examiner has rejected claims 1, 2, 4-6, and 26-28 under 35 U.S.C. §102(e) as being anticipated by Shalaby et al. (U.S. 2002/0160065).

The Examiner's Position

The Examiner alleges that Shalaby, *et al.*, teach using *Nigella sativa* in a composition with antiviral properties to treat infections with hepatitis B virus or hepatitis C virus using about 11.5% to about 34.5% by weight. In addition, the Examiner alleges that Shalaby, *et al.*, disclose the various techniques by which the composition can be administered, such as intranasal, rectal, transdermal, tablets, capsules, patches, and suspensions. Therefore, the Examiner alleges that the teaching of Shalaby, *et al.*, meets the limitations of the present claims and thus anticipates the claimed invention.

Applicants' Invention as Currently Claimed

The present invention, as currently amended and claimed, is directed to a pharmaceutical composition, **consisting essentially of** a therapeutically effective amount of **one** of the botanical plants selected from the group consisting of Actaea rubra, Anemone hepatica,

Anemone nemorosa, Nigella sativa and Ranunculus arvensis, or extracts thereof, and a pharmaceutically acceptable carrier. In another embodiment, the present invention is also drawn to a composition **consisting essentially of** a therapeutically effective amount of **Nigella sativa and Anemone hepatica**, or extracts thereof. In another embodiment, the present invention is also drawn to a pharmaceutical composition consisting essentially of a therapeutically effective amount of Nigella sativa, or an extract thereof and a pharmaceutically acceptable carrier. More particularly, the claims recite that the composition consisting essentially of one of the plants is present in a concentration of not less than 20% weight per volume. The composition may be delivered as a tablet or capsule, or in the form of a liquid or suspension. It may be delivered intramuscularly, subcutaneously, intravenously, intranasally, topically, transdermally, or in the form of a suppository. It may be used to treat hepatitis and to increase the number of immune cells and platelets in patients. In addition, the compositions may be used for treating advanced stage hepatitis patients, characterized as having fibrosis and cirrhosis of the liver as well as for increasing immune cells and platelets in patients.

Claim Amendments and Arguments in Support of Patentability over Shalaby et al.

Applicants respectfully traverse the Examiner's rejection and assert that in order for a rejection under 35 U.S.C. §102 to be proper, the reference(s) must teach each and every element of the invention as claimed. Shalaby et al. do not teach the compositions of the present invention as currently claimed.

Shalaby et al. teach an herbal composition comprising extracts from **a combination of plants**, including the leaves or seeds of Sesbania aegyptiaca, and at least one additional extract selected from the group consisting of Nigella sativa, Cichorium intybus, Cymbopogon proximus, Hemidesmus indicus, Solenostema argel, Rheum officinale and Ecballium elaterium. Further, the compositions comprise at least one auxiliary extract selected from the group consisting of Foeniculum vulgare, Centaurium erythrae, Cynara cardunculus, Inula helenium and Cuminum cyminum. In addition, further herbal compositions are disclosed, comprising a **combination** of extracts from the group consisting of Foeniculum vulgare, Nigella sativa, Centaurium erythrae, Cynara cardunculus, Inula helenium, Solenostema argel, Cichorium intybus, Cymbopogon

proximus, Hemidesmus indicus, Rheum officinale and Cuminum cyminum. Other compositions include a **combination** of extracts from Inula helenium, Centaurium erythrae, Nigella sativa, Sesbania aegyptiaca, Hemidesmus indicus, or from Hemidesmus indicus, Cynara cardunculus, Centaurium erythrae, Foeniculum vulgare, Solenostema argel, Cichorium intybus and Sesbania aegyptiaca. Additional compositions comprise a **combination** of extracts from Nigella sativa, Centaurium erythrae, Sesbania aegyptiaca, Foeniculum vulgare, and Cymbopogon proximus. Further compositions comprise a **combination** of extracts from Hemidesmus indicus, Cynara cardunculus, Centaurium erythrae, Foeniculum vulgare, Solenostema argel, Cichorium intybus, and Sesbania aegyptiaca. Yet further compositions comprise a **combination** of extracts from Rheum Officinale, Cuminum, Inula helenium, Cynara cardunculus, Foeniculum vulgare and Sesbanium aegyptiaca.

Shalaby et al. also teach methods of treating a viral infection by administering a therapeutically effective amount of these compositions.

In order to place the application in condition for allowance, Applicants amend claims 1, 2 and 26 to delete the open-ended language, ie. "comprising", with the phrase "consisting essentially of". Applicant reserves the right to pursue the broader scope of the invention in a further continuation or divisional application.

For example, Applicants amend claim 1 to recite:

"A pharmaceutical composition, consisting essentially of a therapeutically effective amount of one of the botanical plants selected from the group consisting of Actaea rubra, Anemone hepatica, Anemone nemorosa, Nigella sativa, and Ranunculus arvensis, or extracts thereof, and a pharmaceutically acceptable carrier, wherein the one of the botanical plants is present in a concentration of not less than 20% weight per volume."

Furthermore, claim 2 is amended to recite:

"A pharmaceutical composition consisting essentially of a therapeutically effective amount of Anemone hepatica and Nigella sativa, or extracts thereof, and a pharmaceutically acceptable carrier, wherein the Nigella sativa is present in a concentration of not less than 20% weight per volume."

In addition, claim 26 is amended to recite:

"A pharmaceutical composition consisting essentially of a therapeutically effective amount of Nigella sativa, or an extract thereof and a pharmaceutically acceptable carrier, wherein the Nigella sativa is present in a concentration of not less than 20% weight per volume."

Applicants submit that Shalaby et al. **do not teach or suggest** a composition **consisting essentially of** a therapeutically effective amount of **one** of the botanical plants selected from the group consisting of Actaea rubra, Anemone hepatica, Anemone nemorosa, Nigella sativa, and Ranunculus arvensis, or extracts thereof, and a pharmaceutically acceptable carrier, wherein the **one** of the botanical plants is present in a concentration of not less than 20% weight per volume.

In addition, Applicants further assert that Shalaby et al. **do not teach or suggest** a pharmaceutical composition consisting essentially of a therapeutically effective amount of Anemone hepatica and Nigella sativa, or extracts thereof, and a pharmaceutically acceptable carrier, wherein the Nigella sativa is present in a concentration of not less than 20% weight per volume.

Furthermore, Applicants further assert that Shalaby et al. **do not teach or suggest** a pharmaceutical composition consisting essentially of a therapeutically effective amount of Nigella sativa, or an extract thereof and a pharmaceutically acceptable carrier, wherein the Nigella sativa is present in a concentration of not less than 20% weight per volume.

Applicants assert that the amendments to claims 1, 2 and 26, as noted above, render the rejection of the claims under 35 U.S.C. 102(e) moot. That is, Applicants submit that based on the foregoing amendments to the claims, Shalaby et al. **do not teach or suggest** the compositions of the instant invention.

Withdrawal of the rejection under 35 U.S.C. §102(e) is respectfully requested.

Rejection under 35 U.S.C. §103 (a)

The Examiner has maintained the rejection of claims 1 and 4-10 under 35 U.S.C. §103(a) as being unpatentable over Shawkat (U.S. 5,648,089) for the reasons set forth in the previous Office Action.

The Examiner alleges that Shawkat teaches using *Nigella sativa* in an oral herb composition to treat patients diagnosed with active Hepatitis B and Hepatitis C. The Examiner admits that the reference does not specifically teach the ingredients in the dosage forms claimed by Applicants. However, the Examiner alleges that the dosage form or amount of a specific ingredient in a composition is a result effective parameter that a person of ordinary skill in the art would routinely optimize. The Examiner alleges that optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ.

Moreover, the Examiner notes that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art to patentably distinguish the claimed invention from the prior art.

Furthermore, while the Examiner has considered the results of the declaration dated July 1, 2005, the Examiner notes that Applicants did not show any data comparing the high and low doses of the compositions. Therefore, the Examiner alleges that the declaration is not considered supportive of unexpected results.

The Examiner fails to set forth a proper *prima facie* case of obviousness

As noted above, Applicants assert that a rejection under 35 U.S.C. §103 is proper only when a prior art reference alone or in combination with a second prior art reference renders the invention obvious. Applicants further assert that a rejection based upon a combination of references is not proper unless the following three criteria are met: 1) the references in combination teach every single element of the invention as claimed; 2) there must be some suggestion or motivation in the prior art to combine the references to reach the invention as claimed; and 3) there must be a reasonable expectation of success in making the combination to reach the invention as claimed.

The Examiner notes that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The Examiner further alleges that with regards to the dosage form or amount of a specific ingredient, one skilled in the art would be motivated to modify the different dosage forms

or amounts of a specific ingredient to see which form or amount would work best in the invention as taught by the reference.

Applicants respectfully traverse the Examiner's rejection and as noted above, have amended the claims to better clarify what Applicants believe to be the invention. In particular, Applicants have amended claim 1 to recite:

"A pharmaceutical composition, consisting essentially of a therapeutically effective amount of one of the botanical plants selected from the group consisting of Actaea rubra, Anemone hepatica, Anemone nemorosa, Nigella sativa, and Ranunculus arvensis, or extracts thereof, and a pharmaceutically acceptable carrier, wherein the one of the botanical plants is present in a concentration of not less than 20% weight per volume."

Furthermore, claim 2 has also been amended to recite:

"A pharmaceutical composition consisting essentially of a therapeutically effective amount of Anemone hepatica and Nigella sativa, or extracts thereof, and a pharmaceutically acceptable carrier, wherein the Nigella sativa is present in a concentration of not less than 20% weight per volume."

In addition, claim 26 has also been amended to recite:

"A pharmaceutical composition consisting essentially of a therapeutically effective amount of Nigella sativa, or an extract thereof and a pharmaceutically acceptable carrier, wherein the Nigella sativa is present in a concentration of not less than 20% weight per volume."

Applicants submit that it is no more than obvious to try different dosage forms or ingredients, and obvious to try has never been the proper standard for assessing obviousness. Even if, *assuming arguendo*, one of ordinary skill in the art found such dosage forms or ingredients obvious to use, the present invention is still patentable for at least the following four reasons:

1. **Shawkat does not teach or suggest** a pharmaceutical composition **consisting essentially of** a therapeutically effective amount **of one of the botanical plants selected from the group consisting of Actaea rubra, Anemone hepatica, Anemone nemorosa, Nigella sativa and Ranunculus arvensis**, or extracts thereof, and a pharmaceutically acceptable carrier, **wherein the plant compositions must be administered at a**

concentration of not less than 20% weight per volume, as taught and currently claimed by Applicants. Furthermore, there is no teaching by Shawkat that the composition as claimed in amended claim 1 may be used for treating patients having advanced stage hepatitis characterized by fibrosis and cirrhosis wherein the patients are in stage 4-6 of the disease process. In addition, there is simply no teaching or suggestion by Shawkat that the composition as claimed can be used to increase the number of immune cells and platelets in these patients.

2. **Shawkat does not teach or suggest** a pharmaceutical composition **consisting essentially of** a therapeutically effective amount **of Anemone hepatica and Nigella sativa and a pharmaceutically acceptable carrier, wherein the Nigella sativa is present in a concentration of not less than 20% weight per volume.** Furthermore, there is no teaching that the composition as claimed in amended claim 2 may be used for treating patients having advanced stage hepatitis characterized by fibrosis and cirrhosis wherein the patients are in stage 4-6 of the disease process. In addition, there is simply no teaching or suggestion that the composition as claimed can be used to increase the number of immune cells and platelets in patients.

3. **Shawkat does not teach or suggest** a pharmaceutical composition **consisting essentially of** a therapeutically effective amount of Nigella sativa, or an extract thereof and a pharmaceutically acceptable carrier, **wherein the Nigella sativa is present in a concentration of not less than 20% weight per volume**.

In summary, Shawkat does not teach or suggest a pharmaceutical composition consisting essentially of one plant selected from the group consisting of Actaea rubra, Anemone hepatica, Anemone nemorosa, Nigella sativa and Ranunculus arvensis, and a pharmaceutically acceptable carrier, **wherein the one of the botanical plants is present in a concentration of not less than 20% weight per volume.** In addition, **neither Shawkat does not teach or suggest a composition consisting essentially of a therapeutically effective amount of Nigella sativa and Anemone hepatica, or extracts thereof,** and a pharmaceutically acceptable carrier,

wherein the Nigella sativa is present in a concentration of not less than 20% weight per volume. In addition, **Shawkat does not teach or suggest a composition consisting essentially of** a pharmaceutical composition **consisting essentially of** a therapeutically effective amount of Nigella sativa, or an extract thereof and a pharmaceutically acceptable carrier, **wherein the Nigella sativa is present in a concentration of not less than 20% weight per volume**. Moreover, there is no suggestion or motivation for treating stage 4-6 (advanced stage) hepatitis patients having evidence of liver fibrosis and/or cirrhosis using the compositions of the present invention, wherein the plant extracts are present in not less than a 20% concentration, since these unexpected findings were not known until the time of the present invention. Moreover, there is no suggestion or motivation to use the compositions of the present invention for increasing the number of immune cells and platelets in this patient population.

4. **The present compositions provide unexpectedly superior therapeutic effects.** In particular, **no one to date, including Shawkat, has taught or suggested, much less demonstrated, that the compositions as claimed could be useful clinically to improve liver function and liver histopathology, as well as to enhance the immune function in hepatitis patients at a late stage of the hepatitis disease process, particularly when fibrosis and cirrhosis are evident.** Furthermore, the dose used for treating these late stage hepatitis patients differs significantly from the doses of Shawkat, as is evident in the Declarations under 37 C.F.R. §1.132 signed by Hassan Ahmad and Ismail Elchagea, as submitted herewith. These Declarations under 37 CFR 1.132, provide the data in support of the unexpected findings based on the presently claimed compositions. Applicants again assert that the findings were unexpected in that the hepatitis patients under treatment were at such a late stage in the disease process that an actual improvement in clinical parameters and a reversal of the disease process has never been observed with any other current treatment strategy, including that taught by Shawkat. Applicants further attest to the fact that a composition comprising the plant extracts at less than a 20% weight per volume concentration was not effective in this very sick subset of hepatitis patients showing signs of liver cirrhosis and necrosis.

Accordingly, the dosages taught by Shawkat would not prove effective, since a lower concentration, in particular, 10%, was used. The higher doses of the composition as claimed by Applicants of the present invention were necessitated by the advanced stage of the disease for which treatment was desired and for use in this particular subset of patients having advanced stage hepatitis, for which no other treatment options are available. To Applicants' knowledge, this is the only such therapy that is capable of improving liver function and histopathology and of reversing the liver damage observed in this patient population. More particularly, due to the presence of active fibrosis and cirrhosis in these advanced stage hepatitis patients, the lower doses taught by Shawkat would not be effective. In addition, Shawkat has not demonstrated effects of the plant composition as presently claimed, on platelet counts in this patient population. As noted above, the improvement in liver function and histopathology, as well as on the other noted clinical parameters and immune function in this patient population, was not appreciated by Shawkat, since the need for higher doses could not be predicted until the findings of the current invention.

Applicants assert that the Shawkat reference, does not teach or suggest the compositions of the presently claimed invention. **Shawkat does not teach or suggest the presently claimed plant compositions at the concentrations** taught by the Applicants of the present invention. Applicants further assert that the findings of the present application were unexpected given the fact no other therapies or compositions are available to treat or reverse the pathology associated with this late stage of the disease process. Thus, successful treatment of this subset of hepatitis patients, who exhibit cirrhosis and necrosis, with the presently claimed compositions was unexpected due to the inability of existing therapies to aid in the improvement or reversal of liver pathology in this patient population.

Based on the foregoing, withdrawal of the rejection is respectfully requested.

Fees

No fees are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or to credit any overpayments.

Conclusion

Applicants believe that in view of the foregoing, the claims are in condition for allowance. Withdrawal of the rejections is respectfully requested. If a discussion with the undersigned will be of assistance in resolving any remaining issues, the Examiner is invited to telephone the undersigned at (201) 487-5800, ext. 118, to effect a resolution.

Respectfully submitted,

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Attachments: Two Declarations under 37 CFR 1.132 signed by Hassan Ahmad and Ismail Elchagea, Interview Summary